

MAKERERE



UNIVERSITY

**PREVALENCE, RISK FACTORS AND ANTIMICROBIAL
SUSCEPTIBILITY PATTERN OF UROPATHOGENIC
Escherichia Coli AMONG PATIENTS PRESENTING
WITH URINARY TRACT INFECTIONS AT
INTERNATIONAL HOSPITAL, KAMPALA**

BY

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BLT III

**A SPECIAL RESEACH REPORT SUBMITTED TO THE COLLEGE
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DECLARATION AND APPROVAL

I, **Daniel Changa** a student of Biomedical Laboratory Technology at Makerere University, declare that this research report is my own original work and has never been submitted to any institution of learning for any academic award.

Signature:  Date: 26/08/2024

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DEDICATION

This research project is dedicated to my wife Rosemary Naula, my brothers Mubala Job, Stephen Lawrence Gwali, cousins brother Kalinda Emmanuel, my friends especially Naisu Julius, Balya Fred, Bulolo Patrick and lastly to my parents Mr. Kintu Gideon and Mrs. Aidah Ruth Kintu.

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LIST OF ABBREVIATIONS AND ACRONYMS

AST	Antimicrobial susceptibility Testing
CDC	Centre for disease control
CF	Fluoroquinolones
CME	Continuous medical education
ECRFQ	Fluoroquinolone-resistant <i>Escherichia coli</i>
ESBL	Extended Spectrum Beta-lactamase
IDSA	Infectious Diseases Society of America
IHK	International Hospital Kampala
MDR	Multi-drug resistant
UTI	Urinary Tract Infections
WHO	World Health Organization

OPERATIONAL DEFINITIONS

Antibiotic resistance occurs when bacteria change in response to the use of antibiotics and it is bacteria, not humans or animals that become antibiotic-resistant.

Antibiotics are antimicrobial substances used to prevent and treat bacterial infections (WHO, 2010).

Antimicrobial susceptibility testing (AST) is a laboratory procedure performed by medical technologists (clinical laboratory scientists) to identify which antimicrobial regimen is specifically effective for individual patients.

Urinary Tract Infection (UTI) is an infection in any part of the urinary system which includes the kidneys, ureters, bladder and urethra.

ABSTRACT

Urinary tract infections are the most common type of bacterial infection diagnosed today and *Escherichia coli* is the most frequent uropathogenic microorganism isolated with increasing antimicrobial resistance against common antibiotics. A descriptive cross-sectional study was carried out to determine the prevalence, risk factor and susceptibility pattern of uropathogenic *Escherichia coli* among UTI patients at IHK from January-March 2024. Urine samples were cultured on MacConkey agar media and antimicrobial susceptibility of *E. coli* colonies were done using VITEK 2 compact system while structured questionnaires were used to gather data on sociodemographic characteristics and risk factors. The prevalence of *Escherichia coli* was 21.0% while 3.0% had mixed infections and 24.0% of the patients had infections with other organisms isolated. The risk factor associated with *E. coli* infection were female (OR=1.18; CI=1.697-2.025), youth below 30 years (OR=1.83; CI=0.445-1.577) and the unmarried (single) patients (OR=1.69; CI=0.941-3.038). *Escherichia coli* isolates were susceptible to Piperacillin-tazobactam (100%), Nitrofurantoin (94.9%), Co-Amoxycalv (87.4%), Atreonom (79.7%). However, *Escherichia coli* isolates were highly resistant to most antimicrobials, especially Cefixime & cefotaxime at 100%, ceftazidim & ciprofloxacin at 90%, Meropenem (57%) while amoxicillin & Cotrimoxazole at 78.5% and 65.8% respectively. Therefore, the study recommended that; antimicrobial susceptibility be done on all urine sample from UTI patients before prescription of antibiotics, health education of the population at risk to reduce exposure to *Escherichia coli*, only trained personnel to prescribe antibiotics for treatment of UTI and susceptible new drug combinations be used in the treatment of UTI caused by *Escherichia coli* while resistant drugs should not be used for empirical treatment of UTI.

CHAPTER ONE

INTRODUCTION

1.1 Background

Urinary tract infections are the most common type of bacterial infection diagnosed today and the most common bacteria to cause these infections are *Escherichia coli* (Pevzner & Holly, 2022). Worldwide, 150 million people are affected by UTIs each year (WHO, 2021) and studies have identified *Escherichia coli* as the main UTI etiologic agent, with prevalence rates ranging between 60% and 90% depending on the region where the study was carried out and the age range of the enrolled subjects (Gilio, *et al.*, 2013). These infections have also become the most common hospital-acquired infections in Africa, accounting for up to 35% of nosocomial infections and second cause of bacteremia in hospitalized patients in all age groups and sexes, with females accounting for 87.5% of the cases compared with males (71.3%) (K. Gupta *et al.*, 2001).

Urinary tract infection constitutes one of the most frequent consultations in health care facilities in Uganda with women being the most affected mainly with *Escherichia coli* (Marcos, *et al.*, 2014). Other bacteria that have been isolated in urinary tract infection include Gram negative bacteria like, *Enterobacter* species, *Klebsiella* species, *Proteus* species and gram-positive bacteria like *Enterococcus* species, *Staphylococcus saprophyticus*, with *E. coli* being the most common organism (Kothari, 2008). Usually treatment of UTI is empirical, however in view of increasing antimicrobial resistance among uropathogens, antimicrobial susceptibility testing becomes the basis for antimicrobial therapy (Sobel & Kaye, 2010).

Antimicrobial resistance in *Escherichia coli* has become a worrying issue that is increasingly observed in human but also in veterinary medicine worldwide (Poirel, *et al.*, 2018). The rate at which *E. coli* strains are becoming resistant to the vast majority of antibiotics is increasing worldwide and this is because the bacterial species has a great capacity to accumulate resistance genes, mostly through horizontal gene transfer. (Nordmann., 2017).

The ESBLs were initially isolated in the hospital settings however, since 2001, reports of community-acquired infections of ESBLs have started emerging, thus making the epidemiology of infections resulting from ESBL-producing bacteria yet more complex (Koksal, *et al.*, 2019). Additionally, fluoroquinolones or beta-lactams such as cephalosporin are recommended as alternatives for the treatment of UTI and therefore, an awareness of regional susceptibility data regarding *E. coli* (antibiograms) is very important for selecting appropriate empirical antibiotics (Choe, 2018).

1.2 Problem statement

Urinary tract infection is one of the most common bacterial infectious diseases encountered in clinical practice, and it is still increasing at a high rate causing significant morbidity (Marcos, *et al.*, 2014). *Escherichia coli* is the most frequent uropathogenic microorganism causing community acquired urinary tract infections (Marcos, *et al.*, 2014). The antibiotic resistance of *E. coli* is increasing rapidly, causing physicians to hesitate when selecting oral antibiotics and there is increased resistance to beta-lactam antibiotics such as cephalosporin and fluoroquinolones which are the most widely used drugs for the empirical treatment of urinary tract infection (Denise, 2013). Even if there are many different antibiotics on market designed to treat UTI, trainings and CMEs conducted on rational use of these antibiotics, the prevalence of UTI due to *E. coli* and associated antibiotic resistance is still very common at IHK where patients continue to surface with recurrent infection after treatment. Furthermore, there is still no literature documented about the prevalence and antimicrobial susceptibility pattern of *E. coli* at IHK hence the need for the study.

1.3 General objective

To determine the prevalence of *Escherichia coli* causing Urinary Tract Infections and its antibiotic sensitivity pattern among patient presenting with UTI at IHK.

1.3.1 Specific objectives

- i. To determine the prevalence of *Escherichia coli* among patients presenting with UTI at International Hospital Kampala.
- ii. To determine the risk factors associated with *Escherichia coli* among UTI patients at International Hospital Kampala.

- iii. To determine antibiotic sensitivity pattern of *Escherichia coli* isolated from urine of patients presenting with UTI at International Hospital Kampala.

1.3.2 Research questions/hypothesis

- i. What is the prevalence of *Escherichia coli* among patients presenting with UTI at International Hospital Kampala?
- ii. What are the risk factors associated with *Escherichia coli* among UTI patients at International Hospital Kampala?
- iii. What is the antibiotic sensitivity pattern of *Escherichia coli* isolated from urine of patients presenting with UTI at International Hospital Kampala?

1.4 Justification of the study

Prevalence of *Escherichia coli* in UTI is increasing at a high rate among patients seeking medical attention at health facilities in Uganda (Marcos, *et al.*, 2014). If nothing is done to reverse this trend, there will be a constant increase of UTI in the population leading to high rate of infertility, preterm birth among pregnant mothers, or even death. There may also be increased antimicrobial resistance among patients due to poor usage or misuse of these antibiotics which is a major challenge to successful treatment. This study therefore was aimed at determining the prevalence, risk factors and antimicrobial susceptibility pattern of *Escherichia coli* among patients presenting with signs and symptoms of UTI at IHK.

1.5 Significance of the study

The study provided data and information for policy makers and clinicians for proper management of *Escherichia coli* in community acquired urinary tract infections. The findings of the study formed a basis for preliminary decision making on the appropriate line of treatment for UTIs. The study also ensured that clinicians understand the current seriousness of antibiotic-resistant *E. coli*, the mechanisms by which resistance is selected for, and methods that can be used to prevent antibiotic resistance. The study provided information that can help in proper choosing of drugs for imperial treatment of UTI for better outcome. This can also minimize the cost incurred during the treatment of antimicrobial resistant *Escherichia coli* in community acquired UTI and reduce morbidity due to the infections. The data also helped in health education of the population at risk to prevent exposure to conditions that may

predispose them to community acquired urinary tract infections and mitigate the burden of the disease in the community for better quality of life.

CHAPTER TWO

LITERATURE REVIEW

2.1 Urinary Tract Infections (UTI)

Urinary tract infection refers to microbial invasion of the urinary tract by one or more uropathogenic bacteria species, leading to significant bacteriuria and the presence of symptoms such as dysuria (Donkor *et al.*, 2019). UTIs are common infections that happen when bacteria, often from the skin or rectum, enter the urethra, and infect the urinary tract. The infections can affect several parts of the urinary tract, but the most common type is a bladder infection (cystitis) and Kidney infection (pyelonephritis) which is less common, but more serious than bladder infections (CDC, 2022).

An uncomplicated urinary tract infection is that of the bladder and associated structures in which the patients have no structural abnormality and comorbidities, such as diabetes, immunocompromised state, or pregnancy (Tang *et al.*, 2019). Typical symptoms include urinary frequency, urgency, suprapubic discomfort, and dysuria. UTI is one of the most common infections in women but uncommon in circumcised males and therefore by definition, any UTI in male is usually considered complicated (Long *et al.*, 2018).

Many cases of uncomplicated UTIs will resolve spontaneously, without treatment, but many patients seek therapy for symptom relief. Treatment is aimed at preventing the spread to the kidneys or developing into upper tract disease/pyelonephritis, which can cause the destruction of the delicate structures in the nephrons and eventually lead to hypertension (Bull *et al.*, 2018).

Community-acquired uncomplicated urinary tract infections account for a large proportion of infectious diseases and a substantial amount of oral antibiotics is prescribed on a daily basis to treat UTIs in community-based outpatient clinics (Dong, *et al.*, 2018).

2.1.1 *Escherichia coli* in Urinary tract infections

According to the National Kidney Foundation, 80 to 90 percent of UTIs are caused by a bacteria called *Escherichia coli* (*E. coli*). For the most part, *E. coli* lives harmlessly in the gut but it can cause problems if it enters the urinary system, usually from stool

that migrates into the urethra (Riggins *et al.*, 2019). *E. coli* causes the vast majority of UTIs, followed by *Klebsiella*, but other organisms of importance include *Proteus*, *Enterobacter*, and *Enterococcus* (Behzadi *et al.*, 2010).

Escherichia coli often gains entry into the urinary tract via stool thus, women are particularly at risk for UTIs because their urethra sits close to the anus where *E. coli* is present. A woman's urethra is also shorter than a man's giving the bacteria easier access to the bladder where the majority of UTIs occur, and the rest of the urinary tract (Christiano, 2019).

2.2 Prevalence of *Escherichia coli* in community acquired UTI infections

It has been estimated that about six million patients visit outpatient departments (OPD) and about 300,000 are treated in the wards every year for UTI worldwide (Bhat *et al.*, 2011). The causative agents of UTI are developing resistance against antibiotics and treatment costing the global economy in excess of 6 billion dollars (Gonzalez *et al.*, 1999).

The prevalence of UTI has been reported in all age groups and in both sexes. However, it has been estimated that more than 60% women have UTI at least once in their life time (Foxman, *et al.*, 2000). It has also been reported that the rate of the infection is 10.57% higher in sexually active females and teenage girls than males and the most common bacteria involved are *Escherichia coli* (Dromigney, *et al.*, 2005).

UTIs have proven to be a serious challenge for medical professionals due to high incidence, recurrence, complications, diverse etiologic agents, and growing antibiotic resistance (Isaac Odongo *et al.*, 2020). They account for 10–20% of all infections treated in primary care and 30–40% of infections treated in hospitals (Milica, *et al.*, 2017).

Escherichia coli, the predominant organism, observed in the UTI patients has high prevalence in Uganda and there was a significantly high resistance to cefuroxime, ceftazidime, nalidixic acid, and ciprofloxacin (Isaac Odongo *et al.*, 2020). Continuous use of these drugs might most likely be associated with treatment failure and serious antimicrobial resistance.

The study by (Kungu *et al.*, 2020) found that, there was acceptably high sensitivity to cefotaxime/clavulanic acid and nitrofurantoin with *E. coli* being the most prevalent

community-acquired uropathogen. Nevertheless, initial empiric antimicrobial treatment of UTI should consider the significant prevalence of other agents different from *E. coli* in infants < 3 months, the high prevalence of *Staphylococcus saprophyticus* in patients > 10 years and *Proteus mirabilis* in males (Martinez *et al.*, 2013).

Women get urinary tract infections up to 30 times more often than men do and up to 60 percent of women get a UTI at least once in their lives (Yoon & Scott., 2022) and *E. coli* is the most common microorganism isolated in urine of women with UTI (Dong, *et al.*, 2018). Choosing the antimicrobial agent for initial therapy of urinary tract infection (UTI) is usually empirical and should consider the prevalence of uropathogens in different age groups and gender.

According to study done by (Bonten, *et al.*, 2021), the estimated incidence rate of *E. coli* bacteremia was 48 per 100 000 person-years, but this increased considerably with age: rates per 100 000 person-years were >100 in 55-to-75-year-olds and >300 in 75-to-85-year-olds. Overall, *E. coli* accounted for 27% of documented bacteremia episodes: 18% if hospital acquired, 32% if community-onset healthcare associated, and 33% if community acquired. The estimated case fatality rate was 12%. Approximately 44% of episodes were community acquired, 27% community-onset healthcare associated, and 27% hospital acquired. Urinary tract infection (UTI) was the primary source for 53% of episodes.

2.2 Risk factors associated with *Escherichia coli* in UTI infections

Urinary tract infections (UTIs) are serious health affecting problems worldwide. (Bano K *et al.*, 2020) *E. coli*, *E. faecalis*, *K. pneumoniae*, *S. marcescens*, *P. aeruginosa*, *S. saprophyticus*, *S. aureus* and *Proteus mirabilis* are most common bacteria causing UTIs in human beings.- The *E. coli* accounts for approximately 85% of community acquired UTIs and 50% of hospital acquired UTIs (Ramanath *et al.*, 2011). Different factors like age, gender, immuno-suppression and urological instruments may affect prevalence of UTIs. (Naqvi *et al.*, 2010). Catheter-associated UTIs are one of the most dangerous health risks contributing 34% of all health care associated infections (Fink R *et al.*, 2012).

A major risk factor for UTIs is the use of a urinary catheter including manipulation of the urethra, sexual intercourse and the use of spermicides and diaphragms. Frequent

pelvic exams and the presence of anatomical abnormalities of the urinary tract can also predispose one to a UTI (Leslie *et al.*, 2022).

Pathogenic bacteria ascend from the perineum and rectum, predisposing women to urinary tract infections because they have shorter urethras than men, which further contributes to their increased susceptibility to UTIs (Behzadi *et al.*, 2010). Blood-borne bacteria cause very few uncomplicated UTIs with *Escherichia coli* being the most common organism in uncomplicated UTIs by a large margin, followed by Klebsiella (Yamaji *et al.*, 2018). UTIs are very common after a kidney transplant and the two triggers include the use of immunosuppressive drugs and vesicoureteral reflux (Sakamoto *et al.*, 2019). Other risk factors include the use of antibiotics and diabetes mellitus. Recurrences are common, with nearly half getting a second infection within a year. Urinary tract infections occur at least four times more frequently in females than males (Alperin *et al.*, 2019).

Though majority of these UTIs are acquired in the community and are benign in course but in some situations, they greatly affect the general Health and well-being e.g. Urosepsis in elderly, recurrent UTIs in Pregnant females, hospital and catheter associated UTIs, UTIs Affecting female sexual health. Hospital acquired urinary tract infections are considered to be an entirely different group, in terms of etiology, demography, susceptibility profiles and outcome. Though majority of these UTIs are acquired in the community and are benign in course but in some situations, they greatly affect the general Health and well-being e.g. Urosepsis in elderly, recurrent UTIs in Pregnant females, hospital and catheter associated UTIs, UTIs Affecting female sexual health. Hospital acquired urinary tract infections are considered to be an entirely different group, in terms of etiology, demography, susceptibility profiles and outcome.

2.3 Antimicrobial susceptibility of *Escherichia coli* causing UTI

Previous study by (Mathai, *et al.*, 2008) has showed that *E. coli* has varied susceptibility rates to common drugs like quinolones (74.5%), beta-lactams (57.4%), gentamycin (58.2%), co-trimoxazole (48.5%), and nalidixicacid (77.7%). The increasing prevalence of extended spectrum beta lactamase- (ESBL-) producing *E. coli*. Treatment of Multidrug resistance (MDR) *E. coli* causing UTI increases the cost of treatment, hospital stay, morbidity and mortality in patients in Uganda. There are

limited oral options for the treatment of ESBL-producing bacteria associated with lower urinary tract infections (acute cystitis) (Caron et al., 2017). Cotrimoxazole was a typical antibiotic used to treat UTIs, but the resistance of *E. coli* to this drug has markedly increased. According to the literature published in the past decade, in Asia, a 10~15% resistance rate to this drug was reported in Japan (Hayami *et al.*, 2010), with approximately 30% resistance rates observed in China and south Korea (Yang B *et al.*, 2018).

In Europe and the Mediterranean region, the resistance rates of *E. coli* to cotrimoxazole varied but were usually over 15% (Chervet *et al.*, 2017). There was an interesting report wherein the authors emphasized the role of cotrimoxazole in empirical antibiotics because of the recent decrease in the resistance rate to cotrimoxazole in several European countries due to its low prescription rate (Caron *et al.*, 2017). However, it may be not possible to reuse the drug worldwide within the next several years, and close observation of surveillance data will be required.

Antimicrobial susceptibility profiles of uropathogenic *E. coli* are constantly changing, due to modifications in the antibiogram interpretation criteria and antibiotic prescription habits. Rigorous surveillance of resistance rate is necessary to determine appropriate empirical treatment and limit the spread of multiresistant strains (Daoud, *et al.*, 2020).

2.3.1 Antimicrobial resistance of *Escherichia coli* in UTI infection

The emergence and spread of antibiotic-resistant pathogens is a major public health threat. Resistant pathogens especially enterobacteriaceae can withstand lethal doses of antibiotics with various chemical structures and mechanisms of action (Gajdács, 2019). The rate of drug discovery and its development in the 21st century cannot match with the continuous and detrimental change in antibiotic resistance trends (Medina *et al.*, 2016). Pathogens associated with UTI are increasingly changing their features particularly due to self-medication, overuse, and misuse of drugs (Shweta *et al.*, 2014). With the rampant antimicrobial misuse, there is a rise in the newer and more resistant strains of the etiological agents of UTI. Bacterial infections resistant to antibiotics can limit effective treatment rendering bacterial infections difficult to treat including UTI. In low-income countries, there is a reduced access to health care and high cost of second line drugs like nitrofurantoin and amoxicillin-clavulanate which

limits the use of newer broad-spectrum drugs (Akram *et al.*, 2007). The resistance patterns of community-acquired UTI have not been studied exclusively, yet knowledge regarding common uropathogens and their susceptibility patterns to drugs is key in improving prescription decisions (Kaur *et al.*, 2014). Treatment of patients at Mulago hospital is usually carried out empirically and regular laboratory culture and sensitivity tests of urine from UTI patients are limited (Odoki *et al.*, 2019).

A recent study recommended the use of amoxicillin/clavulanate (or amoxicillin plus aminoglycoside), cefixime, ceftibuten, levofloxacin, ciprofloxacin, and fosfomycin as empirical antibiotics against catheter-associated UTIs, whereas recommended regimens for empiric treatment of uncomplicated UTIs were fosfomycin, nitrofurantoin and pivmecillinam (Arpin *et al.*, 2009). However, cultivation should be performed prior to the use of empirical antibiotics, especially in complicated UTIs because atypical and/or MDR microorganisms are more likely to be isolated.

2.3.2 Mechanisms of antimicrobial resistance of *Escherichia coli*

The mechanism of bacterial resistance to cotrimoxazole is due to; drug efflux pumps, the degradation of the antibiotics by enzymes, the alteration of antibiotic binding targets, and the loss of drug entry points, all of which can occur via chromosomal mutations or the acquisition of plasmids (Huovinen, 2001). Chromosomal-mediated resistance decrease in fluoroquinolone uptake and the expression of efflux pumps. Plasmid-encoded proteins which are associated with fluoroquinolones resistance are; Quaternary proteins which decrease topoisomerase-DNA binding and protects enzyme-DNA complexes from quinolones, Aac(6′)-Ib-cr which acetylate the free nitrogen of the C7 ring of the quinolones, and plasmid-encoded efflux pumps such as QepA1 and QepA2 (Hooper *et al.*, 2009)

Fluoroquinolones have a keto acetic acid group where fluoroquinolone–topoisomerase binding is facilitated through a water-metal ion bridge (Aldred *et al.*, 2014). Eventually, fluoroquinolone–topoisomerase complex inhibits topoisomerase activity, and subsequently DNA replication is blocked. Acquisition of resistance to fluoroquinolones is from both chromosome and plasmid. Tetrahydrofolate is required to make both purines and pyrimidines, its synthesis is important for understanding the mechanism of cotrimoxazole, which is a combination of trimethoprim and sulfamethoxazole. Trimethoprim is a structural analog of

dihydrofolic acid that competitively inhibits the synthesis of tetrahydrofolic acid. Sulfamethoxazole, which has a sulfonyl group instead of a carbonyl group, is an analog of para-aminobenzoic acid that competitively inhibits the synthesis of dihydrofolic acid and has been used for over two decades after its first use in 1974 (Torok *et al.*, 2009), this drug has remained the first-line treatment for uncomplicated UTIs in adults (Naber, 2000). Because of the widespread resistance to the drug, cotrimoxazole has been gradually replaced by fluoroquinolones since approximately the year 2000 (Garrison *et al.*, 2001).

2.3.3 Factors for increased antimicrobial resistance of *Escherichia coli* in UTI

In 2011, the Infectious Diseases Society of America (IDSA) recommended that trimethoprim-sulfamethoxazole (cotrimoxazole), nitrofurantoin, fosfomycin, or pivmecillinam be used if local resistance rates of uropathogens causing acute uncomplicated UTIs do not exceed 20% or if the infecting strain is known to be susceptible to these drugs (Dong *et al.*, 2018).

Antibiotic exposure is the most important factor for the selection of antimicrobial resistance Lee *et al.*, (2013) described that increased exposure to fluoroquinolones/cephalosporins made bacteria more resistant to fluoroquinolone/cephalosporins (Lee *et al.*, 2013). Although it is not fully understood in detail how antibiotic resistance arises in microorganisms after their exposure to antibiotics, Baquero suggested that exposure to very low antibiotic concentrations can select for low-level resistant mutants, which serve as stepping stones to the strains with high-level resistance (Baquero, 2001). Similarly, Cantón *et al.*, (2020) suggested that the use of an antibiotic at a concentration capable of preventing the generation of mutants, above the minimal inhibitory concentration, would restrict the emergence of such first-step mutants within a susceptible population Graninger *et al.*, (2006).

Undesirable exposure to antibiotics typically occurs due to the abuse or misuse of antibiotics. In many countries, antibiotics can be obtained over the counter and are as easy to obtain as aspirin and cough medicine (Rocha *et al.*, 1987), which is a major contributing factor to antibiotics abuse.

Recently, a study from India, where resistant rate of antibiotics has been relatively high, investigated antibiotics misuse where participants with limited access to an allopathic doctor, either for logistical or economic reasons, were observed to be more

likely to purchase medications directly from a pharmacy without a prescription (Barker *et al.*, 2017). In the United States, experts estimated that at least half of the human therapeutic use of antibiotics were unnecessary or inappropriate (Harrison *et al.*, 1998).

Colonization has also been suggested to be risk factor for the selection of antimicrobial resistance and most clinical factors associated with colonization and infection by ESBL-producing organisms involve healthcare exposure, such as hospitalization, residence in a long-term care facility, hemodialysis use, and the presence of an intravascular catheter (Jacoby *et al.*, 2005). Studies found the prevalence of ESBL producing organisms was 34 percent overall and 75 percent of individuals (Arcilla *et al.*, 2017) and another report showed an ESBL prevalence of 49.0-64.0% for residents and 5.2-14.5% for staff (Aschbacher *et al.*, 2016).

Environmental hygiene and taking precautions against contact with MDR bacteria can help reduce colonization of pathogenic bacteria (Bush *et al.*, 2010). Once a cluster of resistant bacteria colonizes any part of the human body, it is possible that the bacteria will grow and horizontally transfer plasmid-encoded resistance genes to other susceptible bacteria or to different species Smillie *et al.*, (2010). Equally Harrison *et al.*, (1998) demonstrated that human ingestion of animal and plant food products carries a strong potential for the spread of antibiotic resistance genes via the consumption of antibiotic residues and antibiotic-resistant bacteria.

2.4 Diagnosis of *Escherichia coli* in UTI infections

The diagnosis of a UTI is made from the clinical history (symptoms) and urinalysis with confirmation by a urine culture, but the proper collection of the urine sample is important (Chesbrough, 1990). Collecting urine is critical and therefore, midstream voided specimens are very accurate if the patient follows the correct technique.

The diagnosis of a UTI should not be based solely upon visual inspection of the urine because cloudy urine can be aseptic; the cloudiness can come from protein or calcium phosphate debris in the sample, not necessarily from an infection. Crystal clear urine can be grossly infected and therefore, all urines undergo dipstick testing, which can be done at the bedside. In patients with symptoms of a UTI, a negative dipstick does not rule out the UTI, but positive findings can suggest and help make the diagnosis. There should be microscopic analysis to look for the presence of bacteria and/or white blood

cells (WBC) in the urine (CDC., 2020). Normal urine pH is slightly acidic, with usual values of 5.5 to 7.5, but the normal range is 4.5 to 8.0. A urine pH of 8.5 or 9.0 often indicates urea-splitting organism, such as *Proteus*, *Klebsiella*, or *Ureaplasmaurealyticum*. An alkaline urine pH can signify struvite kidney stones, also known as "infection stones." (Karki & Leslie, 2022).

The nitrate test is the most accurate dipstick test because bacteria must be present in the urine to convert nitrates to nitrites; this takes 6 hours and is why urologists often request the first-morning urine for testing, particularly in males. The specificity of this test is greater than 90%. (Suresh *et al.*, 2021). This test is a direct confirmation of bacteria in the urine, which is a UTI by definition in patients with symptoms. Several bacteria do not convert the nitrates to nitrites, but those are usually involved in complicated UTIs, such as those involving *Enterococcus*, *Pseudomonas*, and *Acinetobacter* (Sabih *et al.*, 2022).

Leukocyte esterase (LE) identifies the presence of WBCs in the urine. The WBCs release the LE, presumably in response to bacteria in the urine. This is why the dipstick LE is a secondary test with a specificity of only 55% for UTIs. LE is good at detecting WBCs in the urine, but WBCs can be in the bladder for other reasons, like inflammatory disorders. Hematuria can be helpful because bacterial infections of the transitional cell lining of the bladder can cause bleeding. This helps distinguish UTI from vaginitis and urethritis, which do not cause blood in the urine (Ganzeboom, *et al.*, 2018).

In many labs, the presence of nitrites or leukocyte esterase will automatically trigger a microscopic evaluation of the urine for bacteria, WBCs, and RBCs. On microscopy, there should be no visible bacteria in uninfected urine, so any bacteria on Gram-stained urine under high field microscopy is highly correlated to bacteriuria and UTIs. A good urine sample with greater than 10 WBC/HPF is abnormal and highly suggestive of a UTI in symptomatic patients (Theofanides, *et al.*, 2018).

Urine should be cultured in all men and all patients with diabetes mellitus, who are immunosuppressed, and women who are pregnant. Classic teaching on urine culture sets the gold standard for infected urine at greater than 10 colony forming units (CFU) per milliliter. Recent literature states that a patient who presents with symptoms and greater than 10 CFU/mL is diagnostic of a urinary tract infection. Urine cultures

rarely help in the emergency department, except with recurrent UTIs, but can make subsequent treatment easier if patients do not respond to the initial antibiotic prescribed (Anger, *et al.*, 2019).

CHAPTER THREE

MATERIALS AND METHODS

3.1 Study design

A descriptive cross sectional study design was used to determine the prevalence, risk factors and susceptibility pattern of *Escherichia coli* in UTI patients at IHK from March to June 2023. Midstream urine samples were collected from 332 patients presenting with signs and symptoms of UTI at the outpatient department of IHK. The samples were cultured, and isolates of *E. coli* and its antimicrobial susceptibility profiles were determined.

3.2 Study area

The study was carried out at International Hospital Kampala (IHK), Uganda. It was a 100-bed private hospital in Kampala, Uganda and was part of the International Medical Group, the largest private healthcare group in Uganda. The hospital, located in Namuwongo, Makindye Division, in southeast Kampala, about 6.5 kilometers (4 mi), by road, southeast of Mulago National Referral Hospital and approximately 3.5 kilometers (2 mi) by road, east of St. Francis Hospital Nsambya. The coordinates of International Hospital Kampala were: 0°18'19.0"N, 32°36'40.0"E (Latitude: 0.305289; Longitude: 32.611112). IHK was selected because it received high cases of UTI especially among the women and therefore antibiotics were highly prescribed for the treatment.

3.3 Study population

Patients presenting with UTI at IHK formed the study population. All outpatients with signs and symptoms of UTI who voluntarily consented to participate were recruited in the study. The qualified study participants were asked to provide midstream urine samples for testing in the laboratory, and information about their age and sex were gathered using structured questionnaires. Urine samples were cultured to determine the presence of *E. coli* organisms and Positive samples for *E. coli* were subjected to antimicrobial susceptibility testing to evaluate their antimicrobial-susceptibility profiles.

3.4 Sample size determination

The sample size was calculated using a 31.5% prevalence reported in Uganda by D. Kabugo, (2016). Using 95% confidence interval and an allowable error of 5%, the sample size (n), was computed using the following formula (Kish & Leslie, 1985)

$$N = \frac{Z^2 (P)(1-P)}{e^2}$$

Z = standard score corresponding to a given confidence level, 95% (1.96)

Z = Z value is confidence level, p = percentage picking a choice, expressed as decimal (0.315) used for sample size needed), e = error, expressed as decimal

$$N = \frac{1.96^2 (0.315)(1-0.315)}{0.05^2}$$

N = 332 samples

A total of 332 patients presenting UTI at IHK were randomly selected to participate in the study.

3.5 Sampling

3.6 Sampling technique

Simple random sampling technique was used to recruit the patients and only those with signs and symptoms of UTI were enrolled in the study. Those who accepted were asked to sign a consent form (appendix III) and structured questionnaire (appendix IV) was administered to individual participants to capture social demographic data. Participants were requested to provide midstream urine sample that was cultured to isolate *E. coli*.

3.6 Data collection

Data was collected from a hospital based testing of 332 participants who met the selection criteria. Researcher-guided questionnaire (appendix III) was also administered and results recorded in data entry form for analysis. Data was collected by testing urine for presence of *E. coli* in UTI infections to establish the prevalence of the uropathogenic *E. coli* and antimicrobial susceptibility testing was carried out on

positive samples. The data was recorded in data collection tools predesigned and analyzed before writing the final report.

3.7 Research study variables

Independent and dependent variables were used to evaluate and to assess the prevalence and risk factors of uropathogenic *E. coli* among patient with UTI. Positive urine culture for *Escherichia coli* in UTI is the dependent variable and the different sociodemographic factors and antibiotics with their susceptibility pattern as independent variables. All variables were analyzed and reported at 95% CI.

3.8 Experiments and procedures on urine detection of pathogenic organisms

Urine samples were tested in laboratory following the principle which states that, urinary tract infections exist when pathogenic microorganisms are detected in the urine, urethra, bladder, kidney or prostate and in most instances growth more than 10^5 organisms/ ml from a midstream clean-catch urine sample indicates infections (SOP-IHKMicro015, 2019). Mid-stream urine sample was collected in clean sterile urine container and examined without delay. Macroscopic examination was done to determine the color, turbidity and presence of blood in the urine. Urine strip was dipped in to the well mixed urine and removed immediately. Excess urine was bled and later the color codes on the stripes were matched with those of the urinestrip container to determine the pH, specific gravity, presence of protein, glucose, leucocytes and positive results were determined using color change. Microscopic examination of the urine sample was done by making a smear on clean slides from the urine deposit and examined under X40 objective to determine presence of bacteria, parasites, pus cells, epithelial cells, crystals and casts. The deposit was then inoculated on blood agar, Sabouraud agar, CLED and MacConkey media using sterile wire loop and the plates were incubated at 35-37°C for 24hours and Vitek 2 system was used to identify the organisms. The VITEK 2 compact system which works on the principle of Matrix-Assisted Laser Desorption/Ionization-time of Flight Mass Spectrometry (MALDI-TOF MS) was used to automatically identify bacteria, yeast and antimicrobial susceptibility using biochemical at predefined Minimum Inhibition Concentration (MIC). The bacteria isolated were noted and antimicrobial susceptibility results were recorded as resistant or susceptible with the percentage of each.

3.9 Quality assurance and control

The quality of the research was assured through pretesting of the research tools including quality control of all tests on urine samples, training of research assistants, giving ample time for data collection, piloting the study, clear inclusion, and exclusion criteria. The investigator ensured the laboratory standard operating procedures (SOPs) were expeditiously followed including proper technique for sample collection, macroscopy, microscopy, biochemical tests and urine culture.

3.10 Data analysis and presentation

First, the raw data was sorted, coded, and organized into an MS Excel spread sheet. The data were exported into a statistical software for social scientists (SPSS) version 25 and analyzed with the help of a biostatistician. Descriptive statistics was used to determine the prevalence of Uropathogenic *E. coli* in UTI and chi-square test and logistic regression were used to determine association between different risk factors and *Escherichia coli* infection which were reported at 95% CI. Antimicrobial susceptibility testing was done and results reported at 95% CI. Chi-square test and logistic analysis were used for comparison and measuring level of association at p-value ≤ 0.05 . The analyzed data was presented in form of tables with frequencies and percentages and figures or charts with narratives under each.

3.11 Ethical considerations

The researcher obtained all approval including permission from the hospital administration to conduct the study at the study area. An informed consent (appendix III) was also obtained from the study participants before proceeding with data collection and they were expected to sign after understanding the benefit of voluntarily participating in the study. Information got from the research participants were handled as confidential and names of the patients were not included on data entry forms, as well as during publication of the research findings. Any of the research participants diagnosed with complication was helped to seek medical attention and those participants who refused to participate were not penalized.

3.12 Dissemination of the research findings

The research finding was delivered to CoVAB for award of Degree in Biomedical Laboratory Technology of Makerere University. And a copy of the report was

delivered to IHK for implementation of the recommendations before publication in a journal.

CHAPTER FOUR

RESULTS

4.1 Sociodemographic characteristics of respondents

Majority of the respondents were female (66.3%), with most being of age 20-30 years (49.4%) and more than half (61.4%) were single. Majority of the respondents were outpatients (97.0%) with 59.6% having history of previous UTI infections while 95.8% had no chronic illness and 57.8% had not used antibiotic recently as shown in table 1 below.

Table 1: Sociodemographic characteristics of the respondents

Variables		Frequency (N=332)	Percentage (%)
Sex	Female	220	66.3
	Male	112	33.7
Age	Teenage (< 20 yrs)	72	21.7
	Youth (20-30 yrs)	164	49.4
	Adult (>30 years)	96	28.9
Education level	Primary	80	24.1
	Secondary	110	33.1
	Tertiary	142	42.8
Marital status	Single	204	61.4
	Married	128	38.6
Type of patient	Outpatients	322	97.0
	Inpatients	10	3.0
Chronic illness	No	318	95.8
	Yes	14	4.2
Previous UT I infection	No	134	40.4
	Yes	198	59.6
Antibiotic use	No	192	57.8
	Yes	140	42.2

4.2 Prevalence of *Escherichia coli* among patients presenting with UTI at IHK

The prevalence of *Escherichia coli* among patients presenting with UTI at IHK was 21.0% while 3% had mixed infections and 24.0% of the patients had infections with other organisms isolated such as *Candida albicans*, *Staphylococcus aureus*, *C. freundii*, *K. pneumonia*, *Streptococcus spp*, and *P. aeruginosa*. The general prevalence of UTI with positive cultures was 48.0% as illustrated in figure 1 below.

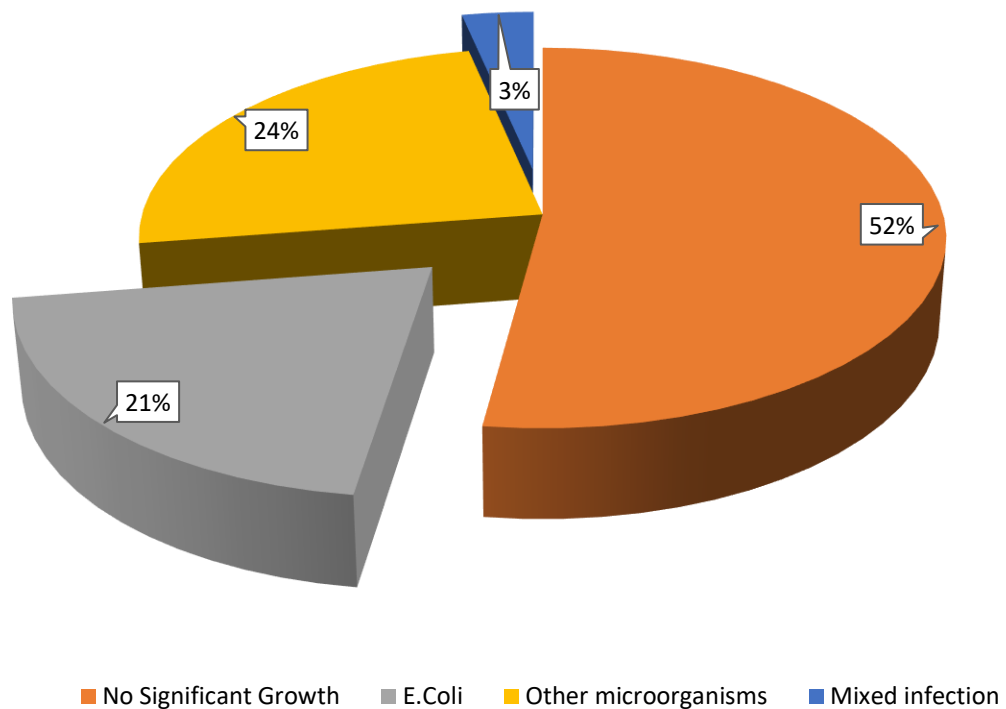


Figure 1: Prevalence of *Escherichia coli* among UTI patients at IHK

4.3 Risk factors associated with *Escherichia coli* infections

The risk factors for *E. coli* infection were; being female (15.1%; $X^2=10.41$, $p=0.022$), being youth below 30 years (12.7%; $X^2=80.70$, $p=0.00$) and being single (12.7%; $X^2=13.01$, $p=0.013$). Other risk factors, although not statistically significant included; low education level (11.2%; $X^2=3.312$, $p=0.191$), previous UTI infections (15.4%; $X^2=4.042$, $p=0.307$), recent antibiotic use (12.3%; $X^2=4.025$, $p=0.145$) and having chronic illness (1.2%; $X^2=0.184$, $p=0.668$) as shown in table 2 below.

Table 2: Risk factors associated with Escherichia coli among UTI patients at IHK

Variables	Category	<i>E. coli</i> + (%)	X²	p-value
Gender	Female	15.1	10.41	0.022
	Male	8.7		
Age	Teenage	3.9	80.701	0.00
	Youth	12.7		
	Adult	7.2		
Marital status	Single	12.7	13.01	0.013
	Married	11.1		
Education level	Primary	11.2	3.312	0.191
	Secondary	8.7		
	Tertiary	3.9		
Previous infection	UTI No	8.4	4.042	0.307
	Yes	15.4		
Antibiotic used	No	11.5	4.025	0.145
	Yes	12.3		
Chronic illness	No	22.6	0.184	0.668
	Yes	1.2		

The risk factors were subjected to logistic regression analysis to determine factors that were independently significant for *E. coli* diagnosis among UTI patients at IHK. Female were 1.18 times more likely to get *E. coli* infection than the male counterparts (OR=1.18; CI=1.697-2.025). The youth below 30 years were 1.83 times more likely to have *E. coli* infection than the adults (OR=1.83; CI=0.445-1.577) and the unmarried (single) patients had 1.69 chance of getting *E. coli* infection than the married (OR=1.69; CI=0.941-3.038).

Table 3: Factors that were independently significant for *E. coli* diagnosis among UTI patients at IHK

Variables	Coefficient	Std. Error	Wald	p-value	OR.	95% CI. for OR	
						Lower Bound	Upper Bound
Single	.525	.299	3.086	0.079	1.69	0.941	3.038
Married					1.0		
Youth < 30yrs	-.177	.323	.301	0.583	1.83	0.445	1.577
Adult <30yrs					1.0		
Female	.172	.272	.401	0.026	1.18	1.697	2.025
Male					1.0		

4.4 Antimicrobial susceptibility pattern of *E. coli* isolated from urine samples

At Minimum Inhibition Concentrations (MIC), *Escherichia coli* isolates were susceptible to Piperacillin-tazobactam (100%), Nitrofurantoin (94.9%), Co-Amoxycalv (87.4%), and Atreonam (79.7%). However, *Escherichia coli* isolates were highly resistant to most antimicrobials such as Cefixime & cefotaxime at 100%, ceftazidin & ciprofloxacin at 90%, Meropenem (57%) while amoxicillin & Cotrimoxazole at 78.5% and 65.8% respectively as shown in table 4 below.

Table 4: Antimicrobial susceptibility pattern of Escherichia coli.

Antibiotic	Concentration in disc (ug/mL)	Resistant	Susceptible
Amikacin	15	41(51.9%)	38(48.1%)
Gentamicin	10	30(38.0%)	49(62.0%)
Cefixime	30	79(100%)	00
Cefotaxime	30	79(100%)	00
Ceftriaxone	30	36(45.6%)	43(54.4%)
Ceftazidim	30	71(90%)	08(10%)
Ciprofloxacin	5	71(90%)	08(10%)
Meropenem	12	45(57%)	34(43.0%)
Piperacillin-tazobactam	32	00	79(100%)
Atreonam	32	16(20.3%)	63(79.7%)
Co-Amoxycalv	32	10(12.7%)	69(87.4%)
Nitrofurantoin	300	04(5.06%)	75(94.9%)
Amoxicillin	32	62(78.5%)	19(21.5%)
Cotrimoxazole	25	52(65.8%)	27(34.2%)

CHAPTER FIVE

DISCUSSION

The purpose of this study was to determine the prevalence, risk factors and antimicrobial susceptibility pattern of uropathogenic *E. coli* among UTI patients at IHK. The study established that the prevalence of *Escherichia coli* was 21.0%, while 3% had mixed infections and the general prevalence of UTI with positive urine culture was 48.0% where 24.0% of the patients had infections with other organisms isolated such as *Candida albicans*, *Staphylococcus aureus*, *C. freundii*, *K. pneumonia*, *Streptococcus spp*, and *P. aeruginosa*.

The prevalence of *Escherichia coli* in this study is higher when compared to those from other studies, such as done by Isaac Odongo *et al.*, (2020) who reported a low prevalence rate of 10% among UTI patients at Mulago National Referral Hospital. Similarly, Kungu *et al.*, (2020) argued that, the prevalence of *Escherichia coli* among outpatient presenting with symptoms of UTI in Uganda was between 10-20% while among inpatient it was between 20-30%. This was because people continue to practice risky behaviors which expose them to *E. coli* infection including poor sanitation and hygiene, having multiple sexual partners, uncontrolled use of antibiotics and douching which compromise their immunity.

However, the prevalence of *Escherichia coli* in this study is lower than those reported in some studies in Uganda such as by Odoki *et al.*, (2019) who reported a higher prevalence of 41.9% in a previous study conducted in patients attending hospitals in Bushenyi district western Uganda. In a similar study by Kabugo *et al.*, (2016) in Mulago hospital, the prevalence of *E. coli* in UTI was found to be 57.5% which was significantly high. Equally, Mwaka *et al.*, (2011) reported a higher prevalence of *Escherichia coli* (50%) among UTI patients at Mulago hospital. The variation in prevalence of *Escherichia coli* in these studies could be attributed to difference in sample size and methods of isolation of the organisms as well as geographical and lifestyle changes including improvement in sanitation and hygiene in the study population as explained by Kabugo *et al.*, (2016).

The risk factors of *Escherichia coli* among patients with UTI at IHK included being female and the female patients had 1.18 chance of getting *E. coli* infection higher than

in the male counterparts. According to Akram *et al.*, (2007) and Hooton and Stamm, (2007), females are at higher risk of UTI because their reproductive anatomy exposes them more to UTI infections than in the male. This could be attributed to a number of factors including close proximity of urethra to the anal opening in females, alteration in the vaginal microflora and the urethral tube being short which make microorganism have easy access to the urinary bladder. Similarly, Dromigney, *et al.*, (2005) reported that, the rate of the infection was 10.57% higher in sexually active females and teenage girls than males and the most common bacteria involved were *Escherichia coli*. Additionally, Akram *et al.*, (2007) reported that, *Escherichia coli* in UTI affects patients in all age groups and sexes, with females accounting for 87.5% of the cases higher as compared with males (71.3%). Equally, Isaac Odongo *et al.*, (2020) reported that, the prevalence was clearly high in females (11.5%) compared with the males (8.3%).

This finding is also consistent with study by Behzadi *et al.*, (2010) who reported that, Pathogenic bacteria ascend from the perineum and rectum, predisposing women to urinary tract infections because they have shorter urethras than men, which further contributes to their increased susceptibility to UTIs. Although all these findings could be true for female, it is also believed that most males don not visit health facilities frequently as do the females which could affect the outcome of the results.

Another risk factor for *E. coli* infection was being youth below 30 years with 1.83 likelihood of getting *E. coli* infection than the adult patients. This could be because the youth and adolescent have multiple sexual partners and are involved in increased sexual activity than the adults exposing them more to UTI infections. Similarly, Odongo *et al.*, (2020) reported higher prevalence of *E. coli* in the age group ≤ 17 years (11.4%) compared with other age groups. And Naqvi *et al.*, (2010) also explained that, different factors like age, gender, immuno-suppression and urological instruments may affect prevalence of UTIs especially among the youth.

Although not statistically significant, those who had low education level (Primary) or the uneducated had higher risk of getting *E. coli* infection compared to the educated. This was because the uneducated had poor sanitation as well as poor hygiene and girls could not clean themselves properly after visiting toilet allowing *Escherichia coli* which is normal flora in the gut to contaminate the vaginal openings and urethra. The

study by Akram *et al.*, (2007) revealed that, the predisposing factors of UTI are accelerated by limited resources, ignorance, poor hygiene, and low socioeconomic status.

Escherichia coli isolated from the urine samples of patients with UTI at IHK were susceptible to drug combinations such as Piperacillin-tazobactam (100%) and Co-Amoxycalv (87.4%). As explained by Arpin *et al.*, (2009), drug combinations have synergistic effect overcoming microorganism antimicrobial resistance mechanism. A study by Akram *et al.*, (2007) found that, combination of cephalosporin and beta lactamase inhibitor in drug formulations possess clinically relevant broad-spectrum antibacterial activity and is highly sensitive against bacteria status. Equally, recent studies recommended the use of drug combination to treat complicated UTI and drugs such as amoxicillin/clavulanate (or amoxicillin plus aminoglycoside) were recommended while cefixime, ceftibuten, levofloxacin, ciprofloxacin, fosfomycin, nitrofurantoin, pivmecillinam and fosfomycin as empirical antibiotics against uncomplicated or catheter-associated UTIs as explained by Arpin *et al.*, (2009).

Escherichia coli was highly susceptible to nitrofurantoin (94.9%) and Atreonom (79.7%) possibly because they were rarely used previously and therefore the organisms were not over exposed to the drugs as also reported by Denise, (2013). Previous studies also reported high susceptibility of *E. coli* to nitrofurantoin and Atreonom although there is slight decline due to recent increase in their use following their recommendation in Uganda Clinical Guidelines 2010.

However, there was high resistance of *Escherichia coli* isolates to most antimicrobials, especially cephalosporin and some fluoroquinolones such as ciprofloxacin that are commonly used in empirical treatment of UTI in outpatients. Cephalosporin such as Cefixime & cefotaxime had 100% resistant rate while *E. coli* were 90% resistant to ceftazidim. The high resistance of this drugs could be attributed to their continuous abuse and over use in empirical treatment of UTI. This finding agrees with that of Choe Lee *et al.*, (2013) who reported that, antibiotic exposure is the most important factor for the selection of antimicrobial resistance and increased exposure to fluoroquinolones/ cephalosporin made bacteria more resistant to the drugs.

Ciprofloxacin which is frequently used for treatment of UTI had 90% resistance which could be due to overuse or misuse of the drug. Similarly, Denise, (2013) reported that, there is increased resistance to beta-lactam antibiotics such as cephalosporin and fluoroquinolones which are the most widely used drugs for the empirical treatment of urinary tract infection.

Escherichia coli isolates were resistant to frequently abused drugs such as Meropenem, amoxicillin & Cotrimoxazole possibly due to over misuse. Previous study by Mathai, *et al.*, (2008) had revealed that, *E. coli* has very high and varied susceptibility rates to common drugs like quinolones, beta-lactams, gentamycin, cotrimoxazole, amoxicillin, nalidixicacid, amikacin. Equally, Denise, (2013) reported that, knowledge of antimicrobial susceptibility of *E. coli* plays a key role in the initial empirical choice of therapy. Therefore, antimicrobial susceptibility should be highly considered before prescription of any antibiotics for treatment of UTI especially those caused by *Escherichia coli*.

However, there were some limitations to the study including small sample size coupled with the cross sectional study design which could not enable follow up of study samples and could limit the generalization of the study findings. Therefore, more studies with larger sample size and longitudinal study design to assess the prevalence and antimicrobial susceptibility pattern of *Escherichia coli* in urinary tract infection must be done in order to evaluate the problem intensively.

CHAPTER SIX

CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusion

The prevalence of *Escherichia coli*, the predominant organism isolated in UTI infection was high. The risk factors for associated with *Escherichia coli* infection included being female, being youth below 30 years and being unmarried (single). *Escherichia coli* isolates were susceptible to new drug combinations such as Piperacillin-tazobactam, Co-Amoxycalv, Atreonam and nitrofurantoin. However, *Escherichia coli* isolates were resistant to most antibiotics especially cephalosporin and fluoroquinolones such as Cefixime, cefotaxime, ceftazidin, ciprofloxacin, Meropenem, amoxicillin, Cotrimoxazole because they were frequently misused in empirical treatment of UTI.

6.2 Recommendations

Antimicrobial susceptibility testing should be done on all urine sample from UTI patients before prescription of antibiotics to reduce development of antimicrobial resistance.

There should be health education of the population to reduce exposure to *Escherichia coli* and other infections including improving sanitation and proper hygiene practices especially among the youth.

Antibiotic use in the treatment UTI should be regulated and only trained personnel to prescribe antibiotics to prevent over exposure of the drugs which may lead to antimicrobial resistance.

New drug combinations which are susceptible for treatment of *Escherichia coli* should be used to prevent resistance.

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APPENDICES

Appendix I: Consent Form

Research Project Title: Prevalence, risk factors and antimicrobial susceptibility Pattern of Uropathogenic *Escherichia coli* among patients presenting with UTI at International Hospital Kampala.

Principal Investigator: CHANGA DANIEL

Makerere University

Tel: 0777 332750/ 0701 141461

Purpose of the study

The purpose of this study was to determine the prevalence, risk factor and susceptibility pattern of *Escherichia coli* causing Urinary Tract Infections in patient presenting with UTI at IHK. The information generated from this study will help to show the disease burden in the population and will help clinicians in management of complicated and uncomplicated UTI caused by E. coli.

What is expected from you?

By participating in this study, was expected to bring urine sample which was tested in the laboratory and the results made known to you by the clinician. They were asked questions about certain aspects of your health and also review your medical records. Should you agree to take part in this study, there was a chance that we may contact you again to re-interview you or do a follow up.

Benefits from the study

There may be no direct benefit from participating in the study. However, there was free culture and sensitivity for urine sample and the results from the study were expected to be beneficial to the participant and the entire population at risk of UTI infections for proper management.

Confidentiality

All the information concerning you shall be kept with utmost confidentiality and only used for this research insofar as the law allows. Only the researcher will have access to it.

Right to Refuse or withdraw from the study

Your participation in the study is entirely voluntary, and you are free to accept or refuse to take part without affecting or jeopardizing your care at IHK. If there is anything that is unclear or you need further information, I shall be delighted to provide it.

Declaration of the participant

I..... have understood the explanation given to me by the researcher, the purpose of the study and my benefits from it. I have accepted to participate in the study without being forced and I have done it on my own will.

..... **Date:**//

Participant Signature

..... **Date:** / /

Research assistant

Whom do I Contact in case of any inquiry?

Researcher: CHANGA DANIEL 0777 332750/ 0701 141461

Research Supervisor:

Appendix II: Questionnaire

A: Social Demographic characteristics of the participants

Participant's ID.....

Age:

Gender 1. Male 2. Female

Marital status 1. Married 2. Single

1) What is your highest level of education?

No formal Education

Primary

Secondary

Tertiary

University

B: Risk factors associated with *Escherichia coli* infection

1. a) Were you diagnosed with UTI infection? Yes No

b) If yes, for how long have been with the infection?

2. Have you taken antibiotics within the last 2 weeks? Yes No

Type of patient

Inpatient Outpatient

Have you ever suffered from a UTI?

1. Yes 2. No

Have you been previously hospitalized?

1. Yes 2. No

Have you used antibiotics in the past 3 months?

1. Yes 2. No

Do you have any chronic disease?

1. Yes 2. No

TEST RESULTS

Urinalysis

.....

Gram stain.....

Organism(s) isolated

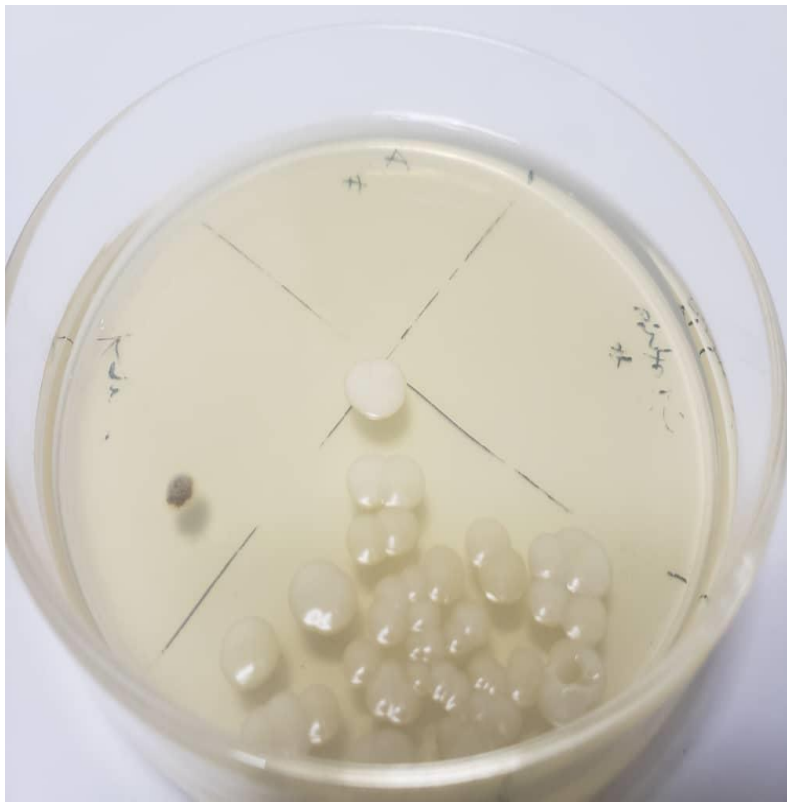
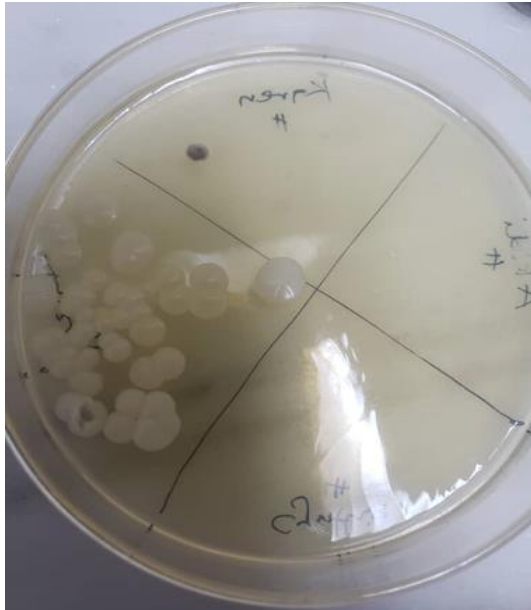
Antimicrobial susceptibility testing.....

.....

.....

Thank you so much for participating in this study and taking your time to answer the
above questions.

Appendix III: Culture plates showing *Esherichia Coli* Isolate and other organisms on SDA arga



Appendix IV: Research Approval

MAKERERE



UNIVERSITY

COLLEGE OF VETERINARY MEDICINE, ANIMAL RESOURCES AND
IOSECURITY

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OFFICE OF THE DEAN

School of Biosecurity, Biotechnical and Laboratory Sciences (SBLs)

Our Ref: 20/U/2053/EVE

Date: 22nd February, 2023

The Head
Department of Microbiology
International Hospital Kampala
Kampala-Uganda

Dear Sir / Madam



RE: INTRODUCTION LETTER FOR MR. DANIEL CHANGA

I hereby introduce to you Mr. Daniel Changa (Reg. No. 20/U/2053/EVE) a finalist student at the College of Veterinary Medicine, Animal Resources and Biosecurity, (CoVAB), Makerere University. He is offering a Bachelor of Biomedical Laboratory Technology (BBLT) programme.

As a finalist student, he proposed to conduct a research study titled; **“PREVALENCE AND ANTIMICROBIAL SUSCEPTIBILITY PATTERN OF UROPATHOGENIC *Echerichia coli* AMONG PATIENTS PRESENTING WITH URINARY TRACT INFECTIONS AT INTERNATIONAL HOSPITAL KAMPALA”**. This is part of the requirements for the award of the Bachelor of Biomedical Laboratory Technology degree.

The purpose of this communication therefore is in strong support of his application to your office for permission to proceed with his research work.

Your support in this regard will be highly appreciated.

Respectfully yours

Dr. Claire Mack Mugasa, (PhD)
DEAN, SBLs

